

HIF-1 INHIBITORS

CROSS REFERENCE TO RELATED APPLICATION

This application claims priority to and benefit of U.S. Provisional Patent Application No. 60/458,218 filed on March 27, 2003, which is incorporated by
5 reference in its entirety.

BACKGROUND

1. Technical Field

The present disclosure is generally directed to inhibitors of Hypoxia Inducible Factor (HIF-1), more particularly to 2,2-dimethylbenzopyran compounds,
10 derivatives thereof, and methods of their use including but not limited to anti-tumor therapies and disorders leading to ischemia (stroke, ischemic heart disease, etc.).

2. Related Art

According to the American Cancer Society, approximately 1.3 million
15 Americans are estimated to be diagnosed with invasive cancer in 2003. The National Cancer Institutes estimates that approximately 8.9 million Americans had a history of cancer in 2003, and approximate 1,500 cancer-related deaths per day are expected in 2003. Because of the staggering number of cancer-related deaths and new cases, new medicines and methods of treatment are needed.
20 Although recent advances have increased our understanding of some of the mechanisms leading to cancer, effective treatments for cancer remain in high demand.

Cancer can be a fatal disease, in part, because cancer can spread or metastasize throughout an organism. Metastasis plays a major role in the morbidity and
25 mortality of breast cancer (Ford, K. et al. Breast cancer screening,

compositions, derivatives, pharmaceutically acceptable salts, prodrugs, or combinations thereof.

Another embodiment provides a method of modulating HIF-1 activity in a cell, for example a eukaryotic cell, by contacting the cell with an HIF-1 inhibiting
5 amount of the disclosed compounds, compositions, derivatives, pharmaceutically acceptable salts, prodrugs, or combinations thereof.

Still another embodiment provides a method of treating or preventing cancer or a tumor in a host by administering to the host a HIF-1 inhibiting amount of the disclosed compounds, compositions, derivatives, pharmaceutically
10 acceptable salts, prodrugs, or combinations thereof.

Another embodiment provides a method of treating psoriasis including administering to the host an HIF- inhibiting amount of the disclosed compounds, compositions, derivatives, pharmaceutically acceptable salts, prodrugs, or combinations thereof. Inhibition of HIF-1 results in the inhibition of HIF-mediated
15 activation of VEGF, which interferes or inhibits VEGF signal transduction involved in psoriasis. It will be appreciated that the disclosed compositions can also be used to treat other VEGF mediated pathologies by interfering or inhibiting HIF-mediated activation of VEGF.

Cancer is a general term for diseases in which abnormal cells divide without
20 control. Cancer cells can invade nearby tissues and can spread through the bloodstream and lymphatic system to other parts of the body. It has been discovered that the administration of an HIF-1 inhibitor to a host, for example a mammal, inhibits or reduces cancer, tumor growth or formation, and the metastasis of tumor cells.

There are several main types of cancer, and the disclosed compositions can be
25 used to treat any type of cancer. For example, carcinoma is cancer that begins in the